REMARKS

This Amendment is being submitted in response to the Office Action mailed on February 14, 2007 in connection with the above-identified application.

Reconsideration of the above-identified application in view of the foregoing amendments and following remarks is respectfully requested.

Claims 1, 3-17, and 19-21 are currently pending and under consideration. Claims 1, 9, and 14 have been amended to recite that the pharmaceutical formulation is non-enterically coated to better define the invention. Support for this amendment can be found on page 4, lines 5-6 of the specification. Claims 10 and 11 have been amended to correct several typographical errors. No new matter has been added as a result of any of these amendments.

Applicants would like to thank the Examiner for withdrawing a number of rejections in view of the amendments and/or remarks contained in the previous Amendment filed on December 6, 2006.

Rejection of Claims 1, 3-17 and 19-21 under 35 U.S.C. 102(e)

Claims 1, 3-17 and 19-21 are rejected under 35 U.S.C. 102(e) as anticipated by U.S. Patent No. 6,489,346 (hereinafter "Phillips II"). The Examiner suggests that Phillips II teaches a non-enteric coated solid pharmaceutical composition comprising a non-enteric coated proton pump inhibitor ("PPI") in a pharmaceutically acceptable carrier and at least one buffering agent, used for treating acid-related gastrointestinal disorders. According to the Examiner, Phillips II teaches that mixtures of the buffering agents can be utilized. Furthermore, Phillips II suggests that the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Applicants respectfully traverse this rejection.

The Phillips II reference merely provides a generic laundry list of possible buffers but in no way discloses or even suggests that the combination of (i) a water-soluble acid neutralizer and (ii) a water-insoluble acid neutralizer can be used to achieve the protectant qualities of the combined acid neutralizers. In particular, the Phillips II reference states that "[A]lthough sodium bicarbonate is the preferred buffering agent employed in the present invention to protect the PPI against acid degradation, many other weak and strong bases (and mixtures thereof) can be utilized" (col. 13, lines 47-50). Furthermore, Phillips II discloses that any weak or strong base, individually or in mixtures, administered when formulated or delivered, (e.g. before, during or after), the PPI, can be used to preserve the bioavailability of the PPI. (col. 13, lines 50-56). A generic listing of strong and weak bases that may be used as possible buffers is then disclosed (col. 13, lines 63 through col. 14, line 14).

The Phillips II reference fails to disclose or suggest the specific combination of both a water-soluble acid neutralizer and water-insoluble acid neutralizer for use as a pharmaceutically acceptable protectant. Thereupon, because Phillips II fails to disclose each and every element of the claimed invention, the rejection of claims 1, 3-17, and 19-21 under 35 U.S.C. Section 102(e) should be withdrawn.

Rejection of Claims 1, 3-17 and 19-21 under 35 U.S.C. Section 103(a)

The Office Action rejects claims 1, 2-17 and 19-21 under 35 U.S.C. Section 103(a) as being unpatentable over Kouchiwa et al. (EP 0 264 259) (hereinafter the "'259 patent") in view of Chen at al. (U.S. Patent No. 6,544,556) (hereinafter "Chen et al."). The Office Action further rejects claims 1, 3-17, and 19-21 under 35 U.S.C. Section 103(a) as being unpatentable over GB 747,293 (hereinafter the "'293 patent") in view of Chen et al. Lastly, the Office Action further rejects claims 1, 3-17, and 19-21 as being unpatentable over Phillips (U.S. Patent No. 5,840,737) (hereinafter "Phillips I") in view of Phillips (U.S. Patent No. 6,489,346) (hereinafter "Phillips II"). Applicants respectfully traverse the rejection.

A) Rejection over the '259 patent in view of Chen et al.

The Examiner states that the '259 patent teaches a stabilized, therapeutic pharmaceutical composition comprising an active ingredient (dihydropyridines) in combination with one or more of sodium carbonate, sodium hydrogen carbonate, calcium carbonate and calcium hydrogen phosphate (See, Office Action, page 5). The Examiner admits that the '259 patent does not teach an acid-labile compound.

With respect to Chen et al., the Examiner states that this reference teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (See, Office Action, page 6). According to the Examiner, pH-buffering substances and alkaline compounds may be mixed with PPIs, and the pharmaceutical compositions are preferably administered orally in oral dosage forms.

Accordingly, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to incorporate acid-labile compounds such as those taught by Chen et al. with the pharmaceutical compositions disclosed in the '259 patent. The Examiner finds the motivation for the combination in that Chen et al. teaches pharmaceutical formulations comprising NSAIDs in combination with acid-labile compounds and teaches that their formulations are effective for treating gastric acid-related diseases. Applicants respectfully traverse this rejection.

The invention as disclosed in the '259 patent is directed to a pharmaceutical composition containing dihydropyridines for the treatment of circulatory diseases. There is no mention of an acid-labile compound throughout the '259 patent, nor is there any suggestion of the use of acid neutralizing compounds, either individually or in combination, as required by the present invention. The '259 patent merely suggests the incorporation of sodium carbonate, sodium hydrogen carbonate, calcium carbonate and/or calcium carbonate but provides no underlying basis except to stabilize the compound. There is no suggestion or reference to neutralizing acid or treating any sort of gastric acid-related diseases within the '259 patent.

Moreover, the invention as disclosed in Chen et al. is specifically directed to an oral dosage form comprising an therapeutically effective amount of an NSAID and a PPI,

wherein the PPI is enterically coated (see col.. 3, line 55-61). The focus of Chen et al. lies in protecting the PPI from coming in contact with acidic conditions, and accordingly focuses on providing an enteric coating around the PPI.

In view of the claims as presently amended, the present invention specifically provides a non-enterically coated formulation that includes the combination of (i) a water-soluble acid neutralizer and (ii) a water-insoluble acid neutralizer. Chen et al. specifically requires an enteric coating, at least in association with the PPI, in order to sufficiently protect the PPI from acidic conditions. Thus, because Chen et al. require the use of an enteric coating, Chen et al. teach away from the present invention through the use of such a coating. In contrast, in the present invention, the combination of the (i) water-soluble acid neutralizer and (ii) water-insoluble acid neutralizer as required by the present invention serves to protect the acid-labile compound from the acidic environment of the stomach. The combination of the acid neutralizers eliminates the need for an enteric coating, accordingly rendering the primary purposes of the Chen et al. invention moot.

Accordingly, there is no suggestion or motivation to combine these two references since the '259 patent does not even suggest the treatment of gastric acid-related disorders and Chen et al. is related to enterically-coated compounds for treating gastric disorders.

B) Rejection over the '293 Patent in view of Chen et al.

The Examiner continues to maintain her rejection that the present invention would be considered unpatentable over the '293 patent in view of Chen et al. In particular, the Examiner states that the '293 patent teaches a pharmaceutical composition comprising a therapeutically effective amount of an acid-labile compound (erythromycin) in combination with acid neutralizers and buffers. (See, Office Action, page 7). According to the Examiner, the '293 patent discloses a number of suitable physiologically acceptable acid neutralizers, which may be used alone or in combination with one another. The Examiner further states that the composition disclosed in the '293 patent provides for adequate blood levels whereby pH levels are effectively maintained. The Examiner does recognize that the '293 patent does not teach 'solid' formulations and is limited to teaching liquid suspensions.

As previously discussed, the Examiner states that Chen et al. teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (See, Office Action, page 7). Moreover, the pharmaceutical compositions are preferably administered orally in oral dosage forms and pH-buffering substances may be mixed with PPIs.

The Examiner therefore concludes that it would have been obvious to one of ordinary skill in the art to incorporate oral, 'solid' dosage forms, such as taught by Chen et al. within the liquid formulations of the '293 patent. Applicants respectfully traverse this rejection.

As discussed previously herein, Chen et al. discloses enterically coated compounds, wherein the enteric coating is used to protect the PPI from acid degeneration. In contrast, the present invention does not require the use of an enteric coating. Accordingly, Applicants submit that there simply is no motivation or suggestion to combine Chen et al. with the '293 patent, since Chen et al. employs an altogether different method to protect a proton pump inhibitor.

Moreover, the '293 patent simply does not teach the <u>combination</u> of a water-soluble acid neutralizer and water-insoluble acid neutralizer. Chen et al. teaches a solid enterically coated proton pump inhibitor, whereas the '293 patent teaches a liquid composition that includes generic acid neutralizers. Accordingly, there is no motivation or even suggestion to combine these two references to achieve the present invention of a solid non-enterically coated pharmaceutical formulation comprising an acid-labile compound and a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer.

C. <u>Rejection over Phillips I in view of Phillips II</u>

The Examiner states that Phillips I teaches a pharmaceutical composition and method for treating and/or preventing gastrointestinal conditions comprising active ingredients of acid-labile compounds (for example, omeprazole, lansoprazole and derivative thereof) and a bicarbonate salt of a Group IA metal, preferably sodium bicarbonate (See Office Action, page 9). The Examiner further states that the composition is used for the treatment of gastrointestinal conditions. The Examiner states that Phillips I teaches a water-

soluble acid-neutralizer, namely, sodium bicarbonate, but admits that Phillips I does not teach a water-insoluble neutralizer or 'solid' pharmaceutical formulations.

The Examiner once again suggests that Phillips II teaches a non-enterically coated solid pharmaceutical composition comprising a non-enteric coated proton-pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent and a method for treating acid-related gastrointestinal disorders comprising administering to a patent the non-enteric coated solid pharmaceutical composition. According to the Examiner, Phillips II teaches that mixtures of the buffering agents can be utilized. Furthermore, Phillips II suggests that the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal.

The Examiner suggests that it would have been obvious to one of ordinary skill in the art to incorporate the solid pharmaceutical formulations of Phillips II which utilize both water soluble- and water-insoluble neutralizers within the pharmaceutical formulations of Philips I. Applicants respectfully traverse this rejection.

The Phillips I reference specifically provides an enterically-coated formulation whereas the Phillips II reference provides a non-enterically coated formation. Accordingly, each of these proposed inventions are distinct from one another and one skilled in the art would not be motivated to combine these references based on the underlying opposite principles. Moreover, as previously suggested, Phillips II merely provides a laundry list of weak and strong bases that may be used as buffers but does not specifically teach the combination of (i) a water-soluble acid neutralizer and (ii) a water-insoluble acid neutralizer. Accordingly, there is not motivation to combine these references to achieve the present invention.

Therefore, Applicants respectfully submit that the rejection of Claims 1, 3-17 and 19-21 under 35 U.S.C. § 103 are improper and should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 102 and 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 04-2223.

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